View metadata, citation and similar papers at core.ac.uk
brought to you by CORE
provided by Elsevier - Publisher Connector

© 2008 International Society of Nephrology

Diuretics should be used as the second-line agent in combination with RAS inhibitors in proteinuric patients with CKD

Kidney International (2008) **74,** 1358; doi:10.1038/ki.2008.466

To the Editor: The Gauging Albuminuria Reduction With Lotrel in Diabetic Patients With Hypertension (GUARD) study,[1] showed that combination of an angiotensin-converting enzyme inhibitor (ACEi) with a diuretic significantly reduced albuminuria more than combination with a calcium channel blocker in patients with type 2 diabetes. As blood pressure (BP) is lowered more in combining an ACEi with a calcium channel blocker, the marked antiproteinuric effects of combining an ACEi with a diuretic cannot be explained by BP control. Thus, at least to reduce proteinuria, a diuretic rather than a calcium channel blocker should be combined with an ACEi or inhibitors of the renin–angiotensin system (RAS).

In contrast to albuminuria reduction, the decline in the glomerular filtration rate (GFR) from the baseline to the end of the 1-year GUARD[1] study was much smaller when an ACEi was combined with a calcium channel blocker than with diuretic. Although this finding is often considered unfavorable for diuretics, we think it opposite. Diuretics suppress tubular sodium reabsorption, making urinary sodium excretion greater than intake. As far as BP, glomerular capillary pressure, GFR, and tubular sodium load remain at the baseline levels, and sodium balance continues negative, resulting in fall in BP. Once BP is lowered, glomerular capillary pressure is also lowered, leading to reductions in both GFR and tubular sodium load. Under diuretic administration, a steady state of sodium balance can be achieved only when the GFR and tubular sodium load are reduced.[2] We believe that the decline in GFR in diuretics reflects lowered glomerular capillary pressure as seen with renin–angiotensin system inhibitors,[3] and therefore may suggest long-term renoprotection. Diuretics should be used as the second-line antihypertensive agent for proteinuric patients with chronic kidney disease, in combination with renin–angiotensin system inhibitors to reduce proteinuria and to preserve renal function.

1. Bakris GL, Toto RD, McCullough PA *et al.* Effects of different ACE inhibitor combinations on albuminuria: results of the GUARD study. *Kidney Int* 2008; **73**: 1303–1309.
2. Fukuda M, Kimura G. Can calcium channel blockers preserve renal function better than diuretics during antihypertensive treatment? *Arch Intern Med* 2005; **165**: 1312.
3. Apperloo AJ, de Zeeuw D, de Jong PE. A short-term antihypertensive treatment-induced fall in glomerular filtration rate predicts long-term stability of renal function. *Kidney Int* 1997; **51**: 793–797.

Michio Fukuda[1] and Genjiro Kimura[1]
[1]*Department of Cardio-Renal Medicine and Hypertension, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan*

Correspondence: *Michio Fukuda, Department of Cardio-Renal Medicine and Hypertension, Nagoya City University Graduate School of Medical Sciences, Mizuho-ku, Nagoya 467-8601, Japan.*
E-mail: m-fukuda@med.nagoya-cu.ac.jp

Response to 'Diuretics should be used as the second-line agent in combination with RAS inhibitors in proteinuric patients with CKD'[1]

Kidney International (2008) **74,** 1358–1359; doi:10.1038/ki.2008.473

Current guidelines support the notion that patients with proteinuric kidney disease should receive a thiazide diuretic as a second agent, if further blood pressure reduction is needed.[2] There are many studies where addition of a nondihydropyridine calcium antagonist, that is, diltiazem provided similar levels of blood pressure reduction to hydrochlorothiazide. Use of this subclass of calcium antagonists is also recommended by current guidelines to reduce blood pressure and proteinuria.[2–4] However, in patients with low levels of proteinuria, that is, generally less than 1 g/day use of any calcium antagonist in the presence of a blocker of the renin–angiotensin system can reduce proteinuria.[5] The Gauging Albuminuria Reduction With Lotrel in Diabetics With Hypertension (GUARD) Study tested the hypothesis that a fixed-dose combination of amlodipine/benazepril is more efficacious in lowering proteinuria than a benazepril/hydrochlorothiazide combination.[6] Although blood pressure was reduced to a greater extent with amlodipine/benazepril, proteinuria was reduced more by benazepril/hydrochlorothiazide. This study is an example where using a surrogate marker effect is misleading. A careful look at the data demonstrates that a significantly greater fall in glomerular filtration rate resulted in a relatively greater fall in proteinuria in the benazepril/hydrochlorothiazide group. Given the better blood pressure reduction without a fall in glomerular filtration rate in the amlodipine/benazepril group, one would have to argue for a calcium antagonist as a second-line agent unless there was a compelling indication for a diuretic, such as edema or volume overload. In short, both thiazide diuretics and calcium antagonists get blood pressure to goal and reduce proteinuria on background therapy that blocks the renin–angiotensin system, so either is a viable option depending on the clinical circumstance.

1. Fukuda M, Kimura G. Diuretics should be used as the second-line agent in combination with RAS inhibitors in proteinuric patients with CKD. *Kidney Int* 2008; doi:10.1038/ki.2008.466.
2. K/DOQI clinical practice guidelines on hypertension and antihypertensive agents in chronic kidney disease. *Am J Kidney Dis* 2004; **43**: 1–290.
3. Materson BJ, Reda DJ, Cushman WC *et al.* Single-drug therapy for hypertension in men. A comparison of six antihypertensive agents

with placebo. The Department of Veterans Affairs Cooperative Study Group on Antihypertensive Agents. *N Engl J Med* 1993; **328**: 914–921.
4. Bakris GL, Weir MR, Secic M *et al.* Differential effects of calcium antagonist subclasses on markers of nephropathy progression. *Kidney Int* 2004; **65**: 1991–2002.
5. Bakris GL, Weir MR, Shanifar S *et al.* Effects of blood pressure level on progression of diabetic nephropathy: results from the renal study. *Arch Intern Med* 2003; **163**: 1555–1565.
6. Bakris GL, Toto RD, McCullough PA *et al.* Effects of different ACE inhibitor combinations on albuminuria: results of the guard study. *Kidney Int* 2008; **73**: 1303–1309.

George L. Bakris[1]
[1]*Hypertensive Diseases Unit, Pritzker School of Medicine, University of Chicago, Chicago, Illinois, USA*
Correspondence: *George L. Bakris, Hypertensive Diseases Unit, Pritzker School of Medicine, University of Chicago, 5841 South Maryland Avenue MC, 1027, Chicago, Illinois 60637, USA. E-mail: gbakris@hotmail.com*

The importance of donor privacy

Kidney International (2008) **74,** 1359; doi:10.1038/ki.2008.468

In their recent editorial on living kidney donation, Maiorano and Schena state that 'several aspects should be discussed by three different players around a circular and not a rectangular table…every player must assume equal responsibility in the decision-making process.'[1] In our view there are three serious problems with this model.

The first is that because the potential donor and recipient would be seated together during the discussion, the results of the potential donor's psychosocial and medical evaluations would be revealed to the potential recipient. Under these circumstances an ambivalent volunteer might not feel free to express her reluctance and the possibility of providing a medical excuse would be eliminated.[2,3] The second concern is that the model requires only a single transplant professional for both the potential donor and recipient. This approach presents a clear conflict of interest for the physician.[4]The recognition of this problem led an international consensus group to conclude that 'transplant centers should make efforts to assure that the medical and psychosocial assessments and the decision to donate incorporates health care professional(s) not involved in the care of the recipient.'[5] Finally, the decision regarding donor suitability should not be shared equally among the three parties. Although it is up to the potential recipient to accept or decline an offer, she should have no say in the determination of donor acceptability.

We agree that determining a person's suitability for living kidney donation involves complex ethical issues[4] but the authors' approach only makes matters worse. While living donation will never be free of ethical concerns, we believe that the Amsterdam Forum's endorsement of independent donor advocates[5] who hold private discussions with potential donors is a major step in the right direction.

1. Maiorano A, Schena FP. The dynamics of kidney donation: viewpoints from the donor, the recipients, and the transplant team. *Kidney Int* 2008; **73**: 1108–1110.
2. Sterner K, Zelikovsky N, Green C *et al.* Psychosocial evaluation of candidates for living related kidney donation. *Pediatr Nephrol* 2006; **21**: 1357–1363.
3. The Authors for the Live Organ Donor Consensus Group. Consensus statement on the live organ donor. *JAMA* 2000; **284**: 2919–2926.
4. Spital A, Taylor JS. Living organ donation: always ethically complex. *Clin J Am Soc Nephrol* 2007; **2**: 203–204.
5. The Ethics Committee of the Transplantation Society. The consensus statement of the amsterdam forum on the care of the live kidney donor. *Transplantation* 2004; **78**: 491–492.

Aaron Spital[1] and James S. Taylor[2]
[1]*Mount Sinai School of Medicine, New York, New York, USA and*
[2]*Department of Philosophy, College of New Jersey, Ewing, New Jersey, USA*
Correspondence: *Aaron Spital, 235 W, 102nd Street 12H, New York, New York 10025, USA. E-mail: aspital@att.net*

Response to 'The importance of donor privacy'

Kidney International (2008) **74,** 1359; doi:10.1038/ki.2008.471

We would like to thank Spital and Taylor[1] for the chance to clarify some important aspects of our Commentary[2] on living kidney donation.

First of all, we think it is important to underline that the 'circular table' should not be seen as a physical entity, where all the participants of the project sit together and discuss the donation issue. In our view, the 'circular table' should be considered as a dynamic interaction among the different 'parts' involved in the process. In addition, we agree with many investigators that the transplant team should involve several experts, 'nephrologists, surgeons, living-kidney-donor coordinators, and social workers', as we specified in our Commentary. This group of experts should mediate the interactions between potential donor and recipient. The sentence about 'equal responsibility in the decision-making process' indicates that each individual involved in the process of living donation has to assume an active part in the decision, expressing doubts, questions, fears, and hopes. In this perspective, the donor's and recipient's risk/benefit profiles should be analyzed by the transplant professional, and discussed with each one individually to clarify that both are fundamental for the correct decision. Finally, public discussion can avoid the danger of financial gain. In this light, we think that the delicate ethical aspects concerning living kidney donation could be correctly faced.

1. Spital A, Taylor JS. The importance of donor privacy. *Kidney Int* 2008; **74**: 1359.
2. Mariano A, Schena FP. The dynamics of kidney donation: viewpoints from the donor, the recipients, and the transplant team. *Kidney Int* 2008; **73**: 1108–1110.

Annamaria Maiorano[1] and Francesco P. Schena[1]
[1]*Emergency and Organ Transplant, University of Bari, Bari, Italy*
Correspondence: *Annamaria Maiorano, Emergency and Organ Transplant, University of Bari, Bari, Italy. E-mail: annamaria.maiorano@gmail.com*